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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/971,960	11/17/97	STILZ	H 026083/0138

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EXAMINER

GAZI,S

ART UNIT

PAPER NUMBER

1616

5

DATE MAILED: 09/25/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No. <b>08/971,960</b>	Applicant(s) <b>Stilz et al.</b>
	Examiner <b>Qazi, Sabiha</b>	Group Art Unit <b>1616</b>

Responsive to communication(s) filed on Nov 17, 1997

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle* 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claim

Claim(s) 1-38 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

Claim(s) \_\_\_\_\_ is/are allowed.

Claim(s) 1-20 and 25-34 is/are rejected.

Claim(s) \_\_\_\_\_ is/are objected to.

Claims 21-24 and 35-38 are subject to restriction or election requirement.

#### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All  Some\*  None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

**— SEE OFFICE ACTION ON THE FOLLOWING PAGES —**

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**First Office Action on Merits**

**Status of the application**

Claims 1-38 are pending. Claims 1-20, and 25-34 are rejected, claims 21-24 and 35-38 are withdrawn from considerations as non elected invention.

***Election/Restriction***

1. Claims 1-38 are generic to a plurality of disclosed patentably distinct species comprising compounds (25, 27, 29, 30, 31, 33), pharmaceutical preparations (claims 1-20, 26, 28, 32, 34), method of use (claims 21-24) and pharmaceutical kits (claims 35-38).
2. The species described in the claims are structurally dissimilar. For example search for formula I when Z is N will not be required for compounds when Z is methylene, Oxygen or sulfur, the ordinary artisan would not consider one such compound to be rendered obvious by the other. Furthermore, Y, Z, D, E and a-h are variables, that make a Markush grouping, and require separate searches. There is no definite core structure.
3. The structurally dissimilar compounds are recognized in the art to represent patentably distinct concepts, and are so divergent in nature as to be separately classified. Burden is

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likewise demonstrated by divergent classification and database search for the entire genus would represent excessive burden on

4. With the election of a specific exemplified Example (e.g. compound or method of use of said compound, etc.), a generic concept will be identified if possible, by the examiner as the inventive group for examination.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification restriction for examination purposes as indicated is proper.

6. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

7. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

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8. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

9. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

10. During a telephonic conversation with Attorney Steven Macbius on 09/18/98, a provisional election was made with traverse to prosecute the invention of species of example 53, (page 75). Affirmation of this election must be made by applicant in responding to this Office action. Claims

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11. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17.

***Claim Rejections - 35 USC § 112***

1. Claims 1-20, 25, 26, 28, 32, 34, 27, 29, 30, 31, 33, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reason apply.

1. Definition of W is confusing. What substituents are part of ring?

2. In the definition of R7 citation of "natural or unnatural amino acid" and "azaamino acid or a dipeptide radical----reduced to -NH-CH2-" is indefinite. It is non limiting.

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***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-20, 25, 26, 28, 32, 34, 27, 29, 30, 31, 33, are rejected under 35 U.S.C. 103(a) as being unpatentable over Zoller et al (WO 95/14008), (US Patent 5,424,293), (US Patent 5,554,594) and (CA 123:314540, abstract of DE 4338944). Zoller et al. disclose imidazoline derivatives as inhibitors of platelet aggregation and osteoclast binding to the bone surfaces. In WO 9514008, see formula (I) on page 1 where similar formula is disclosed as instant formula (I); formula (I) in col. 1, where Y is -(CH<sub>2</sub>)<sub>m</sub>-CO-, Z is O, W is OH, in US'293; see formula I in col. 1 where Y -(CH<sub>2</sub>)<sub>m</sub>-CO-, Z is O, W is OH in US '594; see formula I in abstract where z is NR, b, c, d and f are 0,1, e, g, and h are 0-6. All the above cited references disclose imidazoleline

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derivatives as inhibitors of platelet aggregation and metastasizing of carcinomatous cells etc.

Instant claims are obvious over the above cited references when in instant claims Y is C=O, Z is NR, W=C, B is CH<sub>2</sub>, e, f are 0, D are CR<sub>2</sub>R<sub>3</sub> and E is OH.

The claims differ from the reference by reciting specific species and/or a more limited subgenus than the reference. However, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties.

One having ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render *prima facie* obvious a species falling within the genus. In re Susi, 440 F.2d 442, 445, 169 USPQ 423, 425 (CCPA 1971), followed

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by the Federal Circuit in Merck & Co. V. Biocraft Laboratories, 874 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

2. Claims 1-20, 25, 26, 28, 32, 34, 25, 27, 29, 30, 31, 33, are rejected under 35 U.S.C. 103(a) as being unpatentable over Zoller et al ((CA 123:340969, abstract of WO 95/14008). See formula I, on page I of the reference. See compounds Of RN 170564-97-3 (page 11). Instant compounds can also be homologs of the reference, see compounds of RN 169808-11-1, (page 25), RN 169808-15-5 (page 25) RN 169808-08-6, RN 169808-09-7. These compounds differ from the reference compounds cited above in having methyl groups vs. H. (Copies of the structures with RN cited are enclose).

The prior art of record is drawn to structurally similar compounds which differ from the compounds embraced by the instant claims in that they are homologs. The skilled artisan would have been motivated to modify the teaching of the prior art to prepare homologs because it is recognized in the art that homologs are structurally similar and would be expected to possess similar properties. *Ex parte Henze* (POBA 1948) 83 USPQ 167 .

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors.

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Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Elected species was not found in the prior art. The search was expanded to claims 1-20, 25-34 (others are withdrawn from consideration) These claims have been examined to the extent that they read on the compounds of formula (1), when Z is NR0, Y is C=O, b is 1, c is 1, d is 1, e is 0-6, f is 1, g is 0-6, h is 0-6, E is R10CO, W is C. This is considered a reasonable search according to MPEP 803.02.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha N. Qazi, whose telephone number is (703) 305-3910. The examiner can normally be reached on Monday through Friday from 8 a.m. to 6 p.m. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

*Sabiha N. Qazi*

09/22/98

*S. Mark Clardy*  
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